

From the INTERNATIONAL BUREAU

**PCT**

NOTIFICATION OF TRANSMITTAL  
OF COPIES OF TRANSLATION  
OF THE INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY  
(CHAPTER I OR CHAPTER II  
OF THE PATENT COOPERATION TREATY)  
(PCT Rules 44bis 3(c) and 72.2)

To:

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Date of mailing (day/month/year) 26 October 2006 (26.10.2006)	
Applicant's or agent's file reference PH-2442-PCT	IMPORTANT NOTIFICATION
International application No. PCT/JP2005/006831	International filing date (day/month/year) 31 March 2005 (31.03.2005)
Applicant NAKAO, Kazuwa et al	

## 1. Transmittal of the translation to the applicant.



The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).



The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

## 2. Transmittal of the copy of the translation to the designated or elected Offices.

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

None

The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EG, EP, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

## 3. Reminder regarding translation into (one of) the official language(s) of the elected Office(s).

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Yoshiko Kuwahara
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## PATENT COOPERATION TREATY

## PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY  
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference PH-2442-PCT	FOR FURTHER ACTION	See item 4 below
International application No. PCT/JP2005/006831	International filing date (day/month/year) 31 March 2005 (31.03.2005)	Priority date (day/month/year) 31 March 2004 (31.03.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant NAKAO, Kazuwa		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).
2. This REPORT consists of a total of 8 sheets, including this cover sheet.  
  
In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- |  |   |
|--|---|
| <input checked="" type="checkbox"/> Box No. I    | Basis of the report   |
| <input type="checkbox"/> Box No. II              | Priority  |
| <input checked="" type="checkbox"/> Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability  |
| <input type="checkbox"/> Box No. IV              | Lack of unity of invention  |
| <input checked="" type="checkbox"/> Box No. V    | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> Box No. VI              | Certain documents cited   |
| <input type="checkbox"/> Box No. VII             | Certain defects in the international application  |
| <input checked="" type="checkbox"/> Box No. VIII | Certain observations on the international application   |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis.2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No. +41 22 338 82 70	Date of issuance of this report 19 October 2006 (19.10.2006)
	Authorized officer  Yoshiko Kuwahara  e-mail: pt07@wipo.int

# PATENT COOPERATION TREATY

TRANSLATION

PCT

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing  
(day/month/year)

Applicant's or agent's file reference

**PH-2442-PCT**

FOR FURTHER ACTION

See paragraph 2 below

International application No.

**PCT/JP2005/006831**

International filing date (day/month/year)

**31.03.2005**

Priority date (day/month/year)

**31.03.2004**

International Patent Classification (IPC) or both national classification and IPC

Applicant

**NAKAO, Kazuwa**

1. This opinion contains indications relating to the following items:

- |                                     |              |  |
|-------------------------------------|--------------|--|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the opinion   |
| <input type="checkbox"/>            | Box No. II   | Priority   |
| <input checked="" type="checkbox"/> | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability   |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention   |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Rule 43bis.1(b)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited  |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application   |
| <input checked="" type="checkbox"/> | Box No. VIII | Certain observations on the international application  |

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1(b)(i) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP

Authorized officer

Facsimile No.

Telephone No.

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/JP2005/006831

Box No. 1

Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.  
☐ This opinion has been established on the basis of a translation from the original language into the following language:  
\_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material  
☒ a sequence listing  
☐ table(s) related to the sequence listing
  - b. format of material  
☐ in written format  
☒ in computer readable form
  - c. time of filing/furnishing  
☐ contained in the international application as filed.  
☒ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority for the purposes of search.
3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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Box No. III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 20-31, 51

because:

☒ the said international application, or the said claims Nos. 20-31, 51  
relate to the following subject matter which does not require an international preliminary examination (specify):

The inventions of claims 20-31 and 51 concern treatment of the human body by therapy.  
(PCT Article 34 (4)(a)(i), PCT Rule 67 (1)(iv))

☐ the description, claims or drawings (indicate particular elements below) of said claims Nos. \_\_\_\_\_  
are so unclear that no meaningful opinion could be formed (specify):

☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported  
by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 20-31, 51

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	<input type="checkbox"/> has not been furnished
	<input type="checkbox"/> does not comply with the standard
the computer readable form	<input type="checkbox"/> has not been furnished
	<input type="checkbox"/> does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

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Box No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement		
1. Statement			
Novelty (N)	Claims	1-19, 32-50	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-19, 32-50	NO
Industrial applicability (IA)	Claims	1-19, 32-50	YES
	Claims		NO
2. Citations and explanations:			
<p>This opinion is presented based on the descriptions in the following documents that are listed in the international search report.</p> <p>Document 1: JP 2003-113116 A (Hitokazu NAKAO)</p> <p>Document 2: Yasato KOMATSU et al., Clinical Calcium, 2003, 13(12), p. 1578-1581</p> <p>Document 3: YASODA, A. et al., J. Biol. Chem., 1998, 273(19), p. 11695-11700</p> <p>Document 4: JP 2002-356437 A (Takeda Chemical Industries, Ltd.)</p> <p>Document 5: JP 59-51221 A (Eisai Co., Ltd.)</p> <p>Document 6: WO 02/087620 A1 (Chugai Pharmaceutical Co., Ltd.)</p> <p>Document 7: JP 4-74198 A (Toshiyuki MATSUO)</p> <p>Document 8: JP 4-327598 A (Shionogi &amp; Co., Ltd.)</p> <p>Document 9: JP 11-196873 A (SmithKline Beecham PLC)</p>			
<p>© Claims 1-19 and 40-50</p> <p>Document 1 (CLAIMS and EXAMPLES), document 2 (entire text) and document 3 (entire text, especially ABSTRACT) describe that a substance that activates GC-B is useful in the treatment of achondroplasia diseases. When we compare the inventions of claims 1-19 and 40-50 with the inventions described in these documents, they differ with respect to the fact that in the former the specific application concerns arthritis and proliferation of joint chondrocytes but in the latter this application is not mentioned; the specific sequence of CNP; and the former also includes instances involving at least one NSAID, but in the latter no such instance is mentioned.</p> <p>However, document 3 states that some ingredients that are useful in the treatment of achondroplasia diseases are also useful in the treatment of osteoarthritis (specifically, CLAIMS and EXAMPLES), and likewise it states that this is accomplished by an effect of inducing chondrocytes to differentiate. As noted in document 4, osteoarthritis of the hip and the like are widely known to persons skilled in the art as specific examples of osteoarthritis, and it is widely known from document 5 and the like that many ingredients that are effective in the treatment of osteoarthritis are also effective in the treatment of rheumatoid arthritis. Therefore, this authority finds that no particular inventiveness is required of persons skilled in the art to use the ingredients described in documents 1-3 for the treatment of osteoarthritis and rheumatoid arthritis, or to increase the number of joint chondrocytes.</p> <p>(Continued in supplemental box)</p>			

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

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Box No. VII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1-8, 13, 14, 19, 32-44, 49 and 50

o Claims 1-8, 13, 14, 19, 40-44, 49 and 50

Each of the inventions of these claims concerns a drug, and the active ingredients thereof are restricted exclusively by their function, i. e., a GC-B activator and a NSAID or a cyclooxygenase inhibitor.

However, based on the description therein the chemical structures of substance having these functions are not obvious even to a person skilled in the art. Namely, by merely specifying the function it is unclear which compounds are available as the active ingredient.

According to the statement in the DESCRIPTION of this application, specific results of having these functions were confirmed only when CNP as a GC-B activator and indomethacin as a NSAID or a cyclooxygenase inhibitor were used, and nothing is stated about cases wherein other components are used. Therefore, this authority finds that the same effects as those reported in the DESCRIPTION have not been established in such cases.

Therefore, from the statements in these claims the inventions thereof are unclear, and this authority finds that the DESCRIPTION does not disclose the inventions in a manner sufficiently clear and complete for the inventions to be worked by a person skilled in the art. Thus, the inventions of claims are not sufficiently supported by the DESCRIPTION (PCT Articles 5 and 6).

o Claims 32-39

Each of the inventions of these claims concerns a drug screening method.

Generally speaking, an activity level usable as a specific standard for determination as an indicator should be clearly indicated in an invention relating to a screening method. However, the DESCRIPTION of this application discloses no specific indicator for the screening method. Moreover, when we look at the statements in the EXAMPLES, this authority does not find that a screening was actually performed.

Therefore, this authority finds that the DESCRIPTION does not disclose the inventions of these claims in a manner sufficiently clear and complete for the inventions to be worked by a person skilled in the art. Thus, the inventions of these claims are not sufficiently supported by the DESCRIPTION (PCT Articles 5 and 6).

Since the inventions of these claims are not supported by the disclosures in the DESCRIPTION, it should be noted that in preparing this opinion, prior art documents were searched exclusively based on the cases wherein CNP and its derivatives claimed in claims 9-12 and the specific cyclooxygenase inhibitor claimed in claim 50 were employed as the active ingredient (claims 1-8, 13, 14, 19, 40-44, 49 and 50) and within a reasonable scope based on the disclosures in the DESCRIPTION.

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INTERNATIONAL SEARCHING AUTHORITY

International application No.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box V.

In addition, with respect to the fact that the use of an NSAID is also included, the use of an NSAID, which is a typical anti-inflammatory drug to treat types of inflammatory diseases such as osteoarthritis and rheumatoid arthritis, is a matter of common knowledge to persons skilled in the art as can be seen, for example, from JP 10-251220 A and the like. Therefore, using the inventions of the above claims together with an NSAID is merely conventional practice for persons skilled in the art.

Furthermore, with respect to the sequence of CNP, both CNP-22 and CNP-53 are publicly known as described in the CLAIMS and SEQUENCE DATA of documents 7 and 8. Therefore, this authority finds that the selection thereof presents no particular technical difficulty to persons skilled in the art.

Therefore, based on the descriptions in documents 1-8, the inventions of claims 1-19 and 40-50 lack an inventive step.

○ Claims 32-39

The inventions of these claims differ from the inventions described in documents 1-8 with respect to the fact that they describe screening methods.

However, such screening methods are widely known to persons skilled in the art from document 9 and the like. Therefore, this authority finds that adopting a screening method as an indicator of GC-B activity presents no particular technical difficulty to persons skilled in the art.

Therefore, based on the descriptions in documents 1-9, the inventions of claims 32-39 lack an inventive step.



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INTERNATIONAL SEARCHING AUTHORITY

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Supplemental Box

Continuation of: Box VIII.

Claim 6

According to the statements of claim 6, temporomandibular joint arthrosis is included as osteoarthritis. However, a plurality of prior art documents such as JP 10-509146 A list both temporomandibular joint arthrosis and osteoarthritis, and they do not recognize the inclusion of the former in the latter. In addition, when we examine the statements in the DESCRIPTION (especially page 1), this authority finds no evidence of an inclusive relationship thereof.

This being the case, based on such statements in the CLAIMS, this authority finds that the scope of the target diseases set forth in the CLAIMS is unclear.